

L Number	Hits	Search Text	DB	Time stamp
1	4598	chromosome same (break\$ or fragment\$ or damag\$)	USPAT	2002/06/13 10:02
2	14700	mms or methanesulfonate or bleomycin	USPAT	2002/06/13 10:01
3	2594	interphase\$	USPAT	2002/06/13 10:01
5	0	(chromosome same (break\$ or fragment\$ or damag\$)) same (mms or methanesulfonate or bleomycin) same interphase\$	USPAT	2002/06/13 10:01
6	22	(chromosome same (break\$ or fragment\$ or damag\$)) and (mms or methanesulfonate or bleomycin) and interphase\$	USPAT	2002/06/13 10:02
7	1102	chromosome adj10 (break\$ or fragment\$ or damag\$)	USPAT	2002/06/13 10:02
8	10	(chromosome adj10 (break\$ or fragment\$ or damag\$)) and (mms or methanesulfonate or bleomycin) and interphase\$	USPAT	2002/06/13 10:04
9	36	(chromosome adj10 (break\$ or fragment\$ or damag\$)) same interphase\$	USPAT	2002/06/13 10:08
10	1	(mms or methanesulfonate or bleomycin) same interphase\$	USPAT	2002/06/13 10:07
11	0	((mms or methanesulfonate or bleomycin) same interphase\$)	US-PGPUB	2002/06/13 10:07
12	0	((mms or methanesulfonate or bleomycin) same interphase\$)	DERWENT	2002/06/13 10:07
13	0	(chromosome adj10 (break\$ or fragment\$ or damag\$)) same interphase\$	DERWENT	2002/06/13 10:08

(FILE 'HOME' ENTERED AT 16:31:29 ON 16 MAY 2001)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 16:31:36 ON 16 MAY 2001

L1 55600 S NT OR TDT  
L2 120350 S ALZHEIMER?  
L3 318 S L1 AND L2  
L4 138 DUP REM L3 (180 DUPLICATES REMOVED)  
L5 22 S L4 AND (BREAK? OR TERMI?)  
L6 180 S L3 NOT L4  
L7 8 S L6 AND END LABEL?  
L8 5 DUP REM L7 (3 DUPLICATES REMOVED)

(FILE 'HOME' ENTERED AT 16:59:14 ON 26 APR 2001)

FILE 'MEDLINE, BIOSIS' ENTERED AT 16:59:21 ON 26 APR 2001

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L1      59184 S CHROMOSOM? AND (BREAK? OR FRAGMENT?)
L2      161 S L1 AND (END LABEL?)
L3      114 DUP REM L2 (47 DUPLICATES REMOVED)
L4      3 S L3 AND (INTERPHASE?)
L5      2 S APOTAG
L6      2 DUP REM L5 (0 DUPLICATES REMOVED)
L7      12 S DUPT
L8      9 DUP REM L7 (3 DUPLICATES REMOVED)
L9      3 S L8 AND (END LABEL?)
L10     5813 S TUNEL
L11     30 S L1 AND L10
L12     22 DUP REM L11 (8 DUPLICATES REMOVED)
L13     0 S L12 AND (ALZHEIMER?)
L14     4 S L12 AND (DISEASE?)
L15     4 DUP REM L14 (0 DUPLICATES REMOVED)
L16     30849 S END-LABEL? OR END LABEL? OR TUNEL OR TUNNEL OR DUPT OR DNTP
L17     193 S L16 AND L1
L18     7 S L17 AND (INTERPHASE?)
L19     5 DUP REM L18 (2 DUPLICATES REMOVED)
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L4 ANSWER 2 OF 3 MEDLINE  
 ACCESSION NUMBER: 97329497 MEDLINE  
 DOCUMENT NUMBER: 97329497 PubMed ID: 9185980  
 TITLE: Apoptotic condensations in M-phase cells.  
 AUTHOR: Sit K H; Yin L; Paramanantham R  
 CORPORATE SOURCE: Department of Anatomy, Faculty of Medicine, National  
 University of Singapore, Kent Ridge, Singapore.  
 SOURCE: ANATOMICAL RECORD, (1997 Jun) 248 (2) 149-58.  
 Journal code: 4QM; 0370540. ISSN: 0003-276X.  
 PUB. COUNTRY: United States  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199709  
 ED Entered STN: 19970926  
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 Entered Medline: 19970917

AB BACKGROUND: Apoptosis is a morphologically distinctive form of programmed cell death/cell suicide in which genomic DNA degradation/**fragmentation** and variegated dense chromatin aggregates are characteristic hallmarks that have never been demonstrated in mitotic cells. Perceptions of mutual exclusivity between apoptosis and mitosis imply that M-phase cells cannot be apoptotic. However, in the present study we show apoptotic morphologies in M-phase cells after an acute oxidative stress and endonuclease digestion. METHODS: Degradation of genomic DNA in human Chang liver cells (American Type Culture Collection, ATCC CCL13) was demonstrated by flow cytometric cell-by-cell evaluation

of

(a) propidium iodide intercalative binding to DNA and (b) terminal deoxynucleotidyl transferase (TdT)-mediated 3'OH nick **end labeling** (TUNEL) of **fragmented** DNA. Oxidative stress was imposed by a 30-min prepulse with 200 microM vanadyl(4), which produces hydroxyl free radicals (OH\*), the most reactive of the free radical species. Oxidative stress in the cells was demonstrated by evaluating glutathione-S-transferase (GST)-mediated monochlorobimane-glutathione adduct fluorescence for glutathione content, the main reducing agent of a cell, and methylene blue redox metachromasia, which is a deep color when oxidized and colorless when reduced. Cells with DNA **fragmentation** were highlighted by TUNEL. Apoptotic morphologies were visualized by staining with Giemsa and neutral red dyes and by DNA-propidium iodide binding to chromatin. Direct endonuclease induction of apoptotic morphologies in permeabilized M-phase cells was produced by 1 hr incubation (37 degrees C) with 16 units/ml of micrococcal nuclease. RESULTS: The genomic DNA of proliferative cells, namely in G2/M phase of the cell cycle, was degraded by vanadyl(4) prepulsing and by micrococcal nuclease digestion, concomitantly with DNA **fragmentation** shown by TUNEL. Cytological profiles showed GSH depletion and M-phase cells

with

particularly high oxidative reactivity indicated by methylene blue redox metachromasia. DNA **fragmentation** in M-phase cells was highlighted by TUNEL. Characteristic apoptotic condensations, ranging

from

single-ball condensations to "pulverized" aggregates of a mitotic catastrophe, buddings, and "apoptotic bodies," were found in prophase, metaphase, anaphase, and telophase mitotic cells. The observed separation of condensed chromatin aggregates from the main **chromosome** mass in prophase and metaphase cells could explain micronuclei, linking it

with

apoptosis. Direct endonuclease digestion readily produced apoptotic morphologies in **interphase** and in M-phase cells. **CONCLUSION:** Apoptotic morphologies in M-phase cells can be induced indirectly via oxidative stress or directly via endonuclease activity, which has long been established as a pervading hallmark of apoptosis.

FILE 'MEDLINE' ENTERED AT 07:14:43 ON 14 NOV 2000

L1	249853 S INTERPHASE OR CHROMATIN OR CHROMATID OR NUCLEI?
L2	256453 S BREAK? OR FRAGMENT?
L3	29263 S L1 AND L2
L4	9107 S L1 (P) L2
L5	2953 S L1 (5A) L2
L6	262 S L5 AND (DISEASE? OR ALZHEIMER?)
L7	242387 S INTERPHASE OR CHROMATIN OR NUCLEI?
L8	2167 S L7 (5A) L2
L9	186 S L8 AND (DISEASE?)
L10	60 S L8 AND (CHROMOSOME BREAK?)
L11	36151 S INTERPHASE OR CHROMATIN
L12	1289 S L11 (5A) L2
L13	52 S L12 AND (CHROMOSOME BREAK?)
L14	90 S L12 AND (DISEASE?)
L15	85 S L14 NOT L13
L16	63 S L12 AND (DISEASE?/AB)
L17	817 S L11 (2A) L2
L18	36 S L17 AND DISEASE?/AB

FILE 'STNGUIDE' ENTERED AT 07:41:51 ON 14 NOV 2000

FILE 'MEDLINE' ENTERED AT 07:56:22 ON 14 NOV 2000

FILE 'STNGUIDE' ENTERED AT 07:56:23 ON 14 NOV 2000

FILE 'BIOSIS, CAPLUS, EMBASE, SCISEARCH' ENTERED AT 07:58:34 ON 14 NOV 2000

L19	116 S L18
L20	272 S L17 AND DISEASE
L21	147 S L17 (P) DISEASE
L22	0 S CHROMSOME BREAK? AND (INTERPHASE)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, SCISEARCH' ENTERED AT 08:01:51 ON 14 NOV 2000

L23	382 S CHROMOSOME BREAK? AND (INTERPHASE)
L24	200 DUP REM L23 (182 DUPLICATES REMOVED)
L25	17 S L24 AND (DISEASE OR ALZHEIMER? OR PARKINSON?)
L26	17 S L24 AND (DISEASE? OR ALZHEIMER? OR PARKINSON?)